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Preliminary communication

Organometallic complexes as reagents in peptide synthesis and modification

The masking of peptide bonds by the $[Fe(CO)_3(C_6H_7)]^+$ (Fed) group

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Abstract

The $[Fe(CO)_3(C_6H_7)]^+$ (Fed) species provides a novel masking group for peptide bonds in peptide synthesis. Significant advantages include the rapid one-step mode of attachment, and the facile release and quantitative recovery of the Fed masking group.

Strategies for the protection of reactive amine groups in peptide synthesis are well developed. For example, the t-butoxycarbonyl group (Boc) has been widely used for blocking terminal NH_2 groups, and we recently reported [1] the efficacy of the cyclohexadienyl cation $[Fe(CO)_3(C_6H_7)]^+$ (Fed) in this role. In contrast, methodologies for the masking of peptide bonds have been much less studied [2], despite the potential for overcoming undesirable conformational effects during peptide synthesis.

The recent report by Eckert and Seide [3] of the use of the ferrocenylmethyl (Fem) group for peptide bond masking prompts us to report a similar use of the $[Fe(CO)_3(C_6H_7)]^+$ cation (Fed), which has considerable advantages in terms of ease of formation of the adduct and of the subsequent release of the (Fed) masking group.

Treatment of $[Fe(CO)_3(C_6H_7)]^+$ with equimolar amounts of glycine ethyl ester and diisopropylamine in dichloromethane led to the ca. quantitative in situ formation of the Fed-blocked glycine ethyl ester (I) within a few minutes. Equimolar quantities of t-Boc-analine and the peptide coupling agent DCCl [4*] were then added at $-20\,^{\circ}C$. After allowing the reaction mixture to warm to room temperature

* Reference number with asterisk indicates a note in the list of references.

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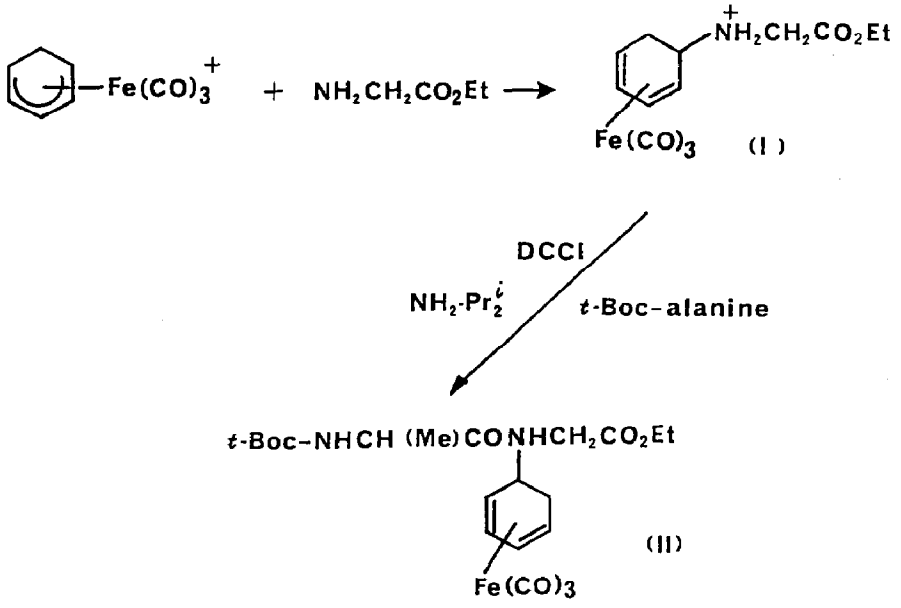

overnight, workup gave the desired peptide (II, 84% yield) in which the Fed group masks the peptide bond (eq. 1).

The masked peptide II was characterised by elemental analyses and its ^{1}H NMR and fast atom bombardment (FAB) mass spectra. Its infrared spectrum in CH_3CN was similar to that of I, showing two characteristic intense ν(CO) bands at 2046 and 1972 cm^{-1}. Its yellow colour and lipophilicity facilitated its purification by column chromatography on silica using hexane/ethyl acetate as eluent. As pointed out earlier [3] for the related Fem masking group, these modified chromophoric and solubility properties imparted to peptides may be of considerable assistance in their purification during synthesis.

A further advantage in employing the Fed masking group is that it can be rapidly and quantitatively removed from the peptide bond by room-temperature treatment with trifluoroacetic acid. The ready recovery of the $[Fe(CO)_3(C_6H_7)]^+$ reagent contrasts with the behaviour of the t-Boc blocking group, which is destroyed upon similar treatment.

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References

1 L.A.P. Kane-Maguire and R. Kanitz, J. Chem. Soc., Chem. Commun., submitted.
2 L. Grehn and U. Ragnarsson, Angew. Chem. Int. Ed. Engl., 24 (1985) 510.
3 H. Eckert and C. Seidel, Angew. Chem. Int. Ed. Engl., 25 (1986) 159.
4 DCCI = dicyclohexylcarbodiimide.